SEQUENCE LISTING

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<110> Bledsoe, Randy, K
     Lambert, Millard, H
     Montana, Valerie, G
     Stewart, Eugene, L
     Xu, H., Eric
<120> STRUCTURE OF A GLUCOCORTICOID RECEPTOR LIGAND BINDING DOMAIN
COMPRISING AND EXPANDED BINDING POCKET AND METHODS EMPLOYING SAME
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Ser Val Leu Ala Gln Glu Arg Gly Asp Val Met Asp Phe Tyr Lys Thr
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| 5 | Leu | Arg | 35 35 | Gly | Ala | act Thr | Val | Lys 40 | Val | Ser | Ala | Ser | Ser 45 | Pro | Ser | Leu | 144 |
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| 40 | aac Asn | ggt Gly | ggc Gly | aat Asn 180 | gtg Val | aaa Lys | ttg Leu | tat Tyr | acc Thr 185 | aca Thr | gac Asp | caa Gln | agc Ser | acc Thr 190 | ttt Phe | gac Asp | 576 |
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| | ctg Leu | ccc | caa Gln 275 | gtg Val | aaa Lys | aca Thr | gaa Glu | aaa Lys 280 | gaa Glu | gat Asp | ttc Phe | atc Ile | gaa Glu 285 | ctc Leu | tgc Cys | acc Thr | 864 |
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| | agc Ser 305 | ttt Phe | cct Pro | gga Gly | gca Ala | aat Asn 310 | ata Ile | att Ile | ggt Gly | aat Asn | aaa Lys 315 | atg Met | tct Ser | gcc Ala | att Ile | tct Ser 320 | 960 |
| 15 | gtt Val | cat His | ggt Gly | gtg Val | agt Ser 325 | acc Thr | tct Ser | gga Gly | gga Gly | cag Gln 330 | atg Met | tac Tyr | cac His | tat Tyr | gac Asp 335 | atg Met | 1008 |
| 20 | aat Asn | aca Thr | gca Ala | tcc Ser 340 | ctt Leu | tct Ser | caa Gln | cag Gln | cag Gln 345 | gat Asp | cag Gln | aag Lys | cct Pro | att Ile 350 | ttt Phe | aat Asn | 1056 |
| 25 | gtc Val | att Ile | cca Pro 355 | cca Pro | att Ile | ccc Pro | gtt Val | ggt Gly 360 | tcc Ser | gaa Glu | aat Asn | tgg Trp | aat Asn 365 | agg Arg | tgc Cys | caa Gln | 1104 |
| 30 | gga Gly | tct Ser 370 | gga Gly | gat Asp | gac Asp | aac Asn | ttg Leu 375 | act Thr | tct Ser | ctg Leu | Gly ggg | act Thr 380 | ctg Leu | aac Asn | ttc Phe | cct Pro | 1152 |
| | ggt Gly 385 | cga Arg | aca Thr | gtt Val | ttt Phe | tct Ser 390 | aat Asn | ggc Gly | tat Tyr | tca Ser | agc Ser 395 | ccc Pro | agc Ser | atg Met | aga Arg | cca Pro 400 | 1200 |
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| 50 | gtg Val | gaa Glu 450 | gga Gly | cag Gln | cac His | aat Asn | tac Tyr 455 | cta Leu | tgt Cys | gct Ala | gga Gly | agg Arg 460 | aat Asn | gat Asp | tgc Cys | atc Ile | 1392 |
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| 35 | gac Asp | caa Gln | tgt Cys | aaa Lys | cac His 645 | atg Met | ctg Leu | tat Tyr | gtt Val | tcc Ser 650 | tct Ser | gag Glu | tta Leu | cac His | agg Arg 655 | ctt Leu | 1968 |
| 40 | cag Gln | gta Val | tct Ser | tat Tyr 660 | gaa Glu | gag Glu | tat Tyr | ctc Leu | tgt Cys 665 | atg Met | aaa Lys | acc Thr | tta Leu | ctg Leu 670 | ctt Leu | ctc Leu | 2016 |
| 45 | tct Ser | tca Ser | gtt Val 675 | cct Pro | aag Lys | gac Asp | ggt Gly | ctg Leu 680 | aag Lys | agc Ser | caa Gln | gag Glu | cta Leu 685 | ttt Phe | gat Asp | gaa Glu | 2064 |
| | att Ile | aga Arg 690 | atg Met | acc Thr | tac Tyr | atc Ile | aaa Lys 695 | gag Glu | cta Leu | gga Gly | aaa Lys | gcc Ala 700 | att Ile | gtc Val | aag Lys | agg Arg | 2112 |
| 50 | gaa Glu 705 | gga Gly | aac Asn | tcc Ser | agc Ser | cag Gln 710 | aac Asn | tgg Trp | cag Gln | cgg Arg | ttt Phe 715 | tat Tyr | caa Gln | ctg Leu | aca Thr | aaa Lys 720 | 2160 |
| 55 | ctc Leu | ttg Leu | gat Asp | tct Ser | atg Met 725 | cat His | gaa Glu | gtg Val | gtt Val | gaa Glu 730 | aat Asn | ctc Leu | ctt Leu | aac Asn | tat Tyr 735 | tgc Cys | 2208 |
| 60 | ttc Phe | caa Gln | aca Thr | ttt Phe 740 | ttg Leu | gat Asp | aag Lys | acc Thr | atg Met 745 | agt Ser | att Ile | gaa Glu | ttc Phe | ccc Pro 750 | gag Glu | atg Met | 2256 |
| | tta Leu | gct Ala | gaa Glu | atc Ile | atc Ile | acc Thr | aat Asn | cag Gln | ata Ile | cca Pro | aaa Lys | tat Tyr | tca Ser | aat Asn | gga Gly | aat Asn | 2304 |

-5-

| | | | 755 | | | | | 760 | | | | | 765 | , | | | |
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| 25 | Ser | Val | Leu | Ala 20 | Gln | Glu | Arg | Gly | Asp 25 | Val | Met | Asp | Phe | Tyr 30 | Lys | Thr | |
| 30 | Leu | Arg | Gly 35 | Gly | Ala | Thr | Val | Lys 40 | Val | Ser | Ala | Ser | Ser 45 | Pro | Ser | Leu | |
| 25 | Ala | Val 50 | Ala | Ser | Gln | Ser | Asp 55 | Ser | Lys | Gln | Arg | Arg 60 | Leu | Leu | Val | Asp | |
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| | Asn | Gly | Gly | Asn 180 | Val | Lys | Leu | Tyr | Thr 185 | Thr | Asp | Gln | Ser | Thr 190 | Phe | Asp |
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| 15 | 225 | | | | | 230 | Glu Pro | | | | 235 | | | | | 240 |
| 20 | Ile | Lys | Asp | Asn 260 | Gly | Asp | Leu | Val | Leu 265 | Ser | Ser | Pro | Ser | Asn 270 | Val | Thr |
| 25 | Leu | Pro | Gln 275 | Val | Lys | Thr | Glu | Lys 280 | Glu | Asp | Phe | Ile | Glu 285 | Leu | Cys | Thr |
| 0.0 | Pro | Gly 290 | Val | Ile | Lys | Gln | Glu 295 | Lys | Leu | Gly | Thr | Val 300 | Tyr | Cys | Gln | Ala |
| 30 | Ser 305 | Phe | Pro | Gly | Ala | Asn 310 | Ile | Ile | Gly | Asn | Lys 315 | Met | Ser | Ala | Ile | Ser 320 |
| 35 | Val | His | Gly | Val | Ser 325 | Thr | Ser | Gly | Gly | Gln 330 | Met | Tyr | His | Tyr | Asp 335 | Met |
| 40 | Asn | Thr | Ala | Ser 340 | Leu | Ser | Gln | Gln | Gln 345 | Asp | Gln | Lys | Pro | Ile 350 | Phe | Asn |
| 45 | Val | Ile | Pro 355 | Pro | Ile | Pro | Val | Gly 360 | Ser | Glu | Asn | Trp | Asn 365 | Arg | Cys | Gln |
| 50 | Gly | Ser 370 | Gly | Asp | Asp | Asn | Leu 375 | Thr | Ser | Leu | Gly | Thr 380 | Leu | Asn | Phe | Pro |
| 50 | Gly 385 | Arg | Thr | Val | Phe | Ser 390 | Asn | Gly | Tyr | Ser | Ser 395 | Pro | Ser | Met | Arg | Pro 400 |
| 55 | Asp | Val | Ser | Ser | Pro 405 | Pro | Ser | Ser | Ser | Ser 410 | Thr | Ala | Thr | Thr | Gly 415 | Pro |
| 60 | Pro | Pro | Lys | Leu 420 | Cys | Leu | Val | Cys | Ser 425 | Asp | Glu | Ala | Ser | Gly 430 | Cys | His |
| | Tyr | Gly | Val | Leu | Thr | Cys | Gly | Ser | Cys | Lys | Val | Phe | Phe | Lys | Arg | Ala |

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| | Thr | Pro 530 | Thr | Leu | Val | Ser | Leu 535 | Leu | Glu | Val | Ile | Glu 540 | Pro | Glu | Val | Leu |
| 25 | Tyr 545 | Ala | Gly | Tyr | Asp | Ser 550 | Ser | Val | Pro | Asp | Ser 555 | Thr | Trp | Arg | Ile | Met 560 |
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| 35 | Trp | Ala | Lys | Ala 580 | Ile | Pro | Gly | Phe | Arg 585 | Asn | Leu | His | Leu | Asp 590 | Asp | Gln |
| 40 | Met | Thr | Leu 595 | Leu | Gln | Туг | Ser | Trp 600 | Met | Phe | Leu | Met | Ala 605 | Phe | Ala | Leu |
| | Gly | Trp 610 | Arg | Ser | Tyr | Arg | Gln 615 | Ser | Ser | Ala | Asn | Leu 620 | Leu | Cys | Phe | Ala |
| 45 | Pro 625 | Asp | Leu | Ile | Ile | Asn 630 | Glu | Gln | Arg | Met | Thr 635 | Leu | Pro | Cys | Met | Tyr 640 |
| 50 | Asp | Gln | Cys | Lys | His 645 | Met | Leu | Tyr | Val | Ser 650 | Ser | Glu | Leu | His | Arg 655 | Leu |
| 55 | Gln | Val | Ser | Туr 660 | Glu | Glu | Tyr | Leu | Cys 665 | Met | Lys | Thr | Leu | Leu 670 | Leu | Leu |
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| 5 | 705 | GTÀ | ASII | ser | ser | 710 | Asn | Trp | Gln | Arg | Phe 715 | Tyr | Gln | Leu | Thr | Lys 720 | |
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| | Leu | Leu | Asp | Ser | Met 725 | His | Glu | Val | Val | Glu 730 | Asn | Leu | Leu | Asn | Tyr 735 | Cys | |
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| 45 | Met 1 | | | | | tca Ser | | | | | | gaa Glu | | | | | 48 |
| 45 | 1 agt | Asp gtg | Ser | Lys gct | Glu 5 cag | | Leu agg | Thr gga | Pro gat | Gly 10 gtg | Arg atg | Glu gac | Glu ttc | Asn tat | Pro 15 aaa | Ser | 48 96 |
| 45 50 | agt Ser | Asp gtg Val aga | Ser ctt Leu gga | Lys gct Ala 20 gga | Glu 5 cag Gln gct | Ser gag | Leu agg Arg | Thr gga Gly aag | Pro gat Asp 25 gtt | Gly 10 gtg Val tct | Arg atg Met | Glu gac Asp | Glu ttc Phe tca | Asn tat Tyr 30 | Pro 15 aaa Lys tca | Ser acc Thr | |
| | agt Ser cta Leu | Asp gtg Val aga Arg | ctt Leu gga Gly 35 | Lys gct Ala 20 gga Gly | Glu 5 cag Gln gct Ala | Ser gag Glu act | Leu agg Arg gtg Val | Thr gga Gly aag Lys 40 tcc | Pro gat Asp 25 gtt Val | Gly 10 gtg Val tct Ser | Arg atg Met gcg Ala cga | Glu gac Asp tct Ser | Clu ttc Phe tca Ser 45 | Asn tat Tyr 30 ccc Pro | Pro 15 aaa Lys tca Ser | ser acc Thr ctg Leu gat | 96 |
| 50 | agt Ser cta Leu gct Ala | Asp gtg Val aga Arg gtc Val 50 cca | ctt Leu gga Gly 35 gct Ala | Lys gct Ala 20 gga Gly tct Ser | Glu 5 cag Gln gct Ala caa Gln | gag Glu act Thr | agg Arg gtg Val gac Asp 55 | Thr gga Gly aag Lys 40 tcc Ser aat | Pro gat Asp 25 gtt Val aag Lys | Gly 10 gtg Val tct Ser cag Gln | atg Met gcg Ala cga Arg | gac Asp tct Ser aga Arg 60 | ttc Phe tca Ser 45 ctt Leu | Asn tat Tyr 30 ccc Pro ttg Leu ctg | Pro 15 aaa Lys tca Ser gtt Val | acc Thr ctg Leu gat Asp | 96 144 |

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| 10 | tcc Ser | tcg Ser | ggg Gly 115 | gaa Glu | aca Thr | gac Asp | tta Leu | aag Lys 120 | ctt Leu | ttg Leu | gaa Glu | gaa Glu | agc Ser 125 | att Ile | gca Ala | aac Asn | | 384 |
| | ctc Leu | aat Asn 130 | agg Arg | tcg Ser | acc Thr | agt Ser | gtt Val 135 | cca Pro | gag Glu | aac Asn | ccc Pro | aag Lys 140 | agt Ser | tca Ser | gca Ala | tcc Ser | | 432 |
| 15 | act Thr 145 | gct Ala | gtg Val | tct Ser | gct Ala | gcc Ala 150 | ccc Pro | aca Thr | gag Glu | aag Lys | gag Glu 155 | ttt Phe | cca Pro | aaa Lys | act Thr | cac His 160 | | 480 |
| 20 | tct Ser | gat Asp | gta Val | tct Ser | tca Ser 165 | gaa Glu | cag Gln | caa Gln | cat His | ttg Leu 170 | aag Lys | ggc Gly | cag Gln | act Thr | ggc Gly 175 | acc Thr | ! | 528 |
| 25 | aac Asn | ggt Gly | ggc Gly | aat Asn 180 | gtg Val | aaa Lys | ttg Leu | tat Tyr | acc Thr 185 | aca Thr | gac Asp | caa Gln | agc Ser | acc Thr 190 | ttt Phe | gac Asp | | 576 |
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| 35 | aat Asn | gag Glu 210 | agt Ser | cct Pro | tgg Trp | aga Arg | tca Ser 215 | gac Asp | ctg Leu | ttg Leu | ata Ile | gat Asp 220 | gaa Glu | aac Asn | tgt Cys | ttg Leu | • | 672 |
| | ctt Leu 225 | tct Ser | cct Pro | ctg Leu | gcg Ala | gga Gly 230 | gaa Glu | gac Asp | gat Asp | tca Ser | ttc Phe 235 | ctt Leu | ttg Leu | gaa Glu | gga Gly | aac Asn 240 | · | 720 |
| 40 | tcg Ser | aat Asn | gag Glu | gac Asp | tgc Cys 245 | aag Lys | cct Pro | ctc Leu | att Ile | tta Leu 250 | ccg Pro | gac Asp | act Thr | aaa Lys | ccc Pro 255 | aaa Lys | - | 768 |
| 45 | att Ile | aag Lys | gat Asp | aat Asn 260 | gga Gly | gat Asp | ctg Leu | gtt Val | ttg Leu 265 | tca Ser | agc Ser | ccc Pro | agt Ser | aat Asn 270 | gta Val | aca Thr | 8 | 316 |
| 50 | ctg Leu | ccc Pro | caa Gln 275 | gtg Val | aaa Lys | aca Thr | gaa Glu | aaa Lys 280 | gaa Glu | gat Asp | ttc Phe | atc Ile | gaa Glu 285 | ctc Leu | tgc Cys | acc Thr | 8 | 364 |
| 55 | cct Pro | ggg Gly 290 | gta Val | att Ile | aag Lys | caa Gln | gag Glu 295 | aaa Lys | ctg Leu | ggc Gly | aca Thr | gtt Val 300 | tac Tyr | tgt Cys | cag Gln | gca Ala | Š | 912 |
| - | agc Ser 305 | ttt Phe | cct Pro | gga Gly | gca Ala | aat Asn 310 | ata Ile | att Ile | ggt Gly | aat Asn | aaa Lys 315 | atg Met | tct Ser | gcc Ala | att Ile | tct Ser 320 | 9 | 960 |
| 60 | gtt Val | cat His | ggt Gly | gtg Val | agt Ser 325 | acc Thr | tct Ser | gga Gly | gga Gly | cag Gln 330 | atg Met | tac Tyr | cac His | tat Tyr | gac Asp 335 | atg Met | 10 | 008 |

| | aat Asn | aca Thr | gca Ala | tcc Ser 340 | ctt Leu | tct Ser | caa Gln | cag Gln | cag Gln 345 | gat Asp | cag Gln | aag Lys | cct Pro | att Ile 350 | ttt Phe | aat Asn | 1056 |
|----|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|------|
| 5 | gtc Val | att Ile | cca Pro 355 | cca Pro | att Ile | ccc Pro | gtt Val | ggt Gly 360 | tcc Ser | gaa Glu | aat Asn | tgg Trp | aat Asn 365 | agg Arg | tgc Cys | caa Gln | 1104 |
| 10 | gga Gly | tct Ser 370 | gga Gly | gat Asp | gac Asp | aac Asn | ttg Leu 375 | act Thr | tct Ser | ctg Leu | Gly | act Thr 380 | ctg Leu | aac Asn | ttc Phe | cct Pro | 1152 |
| 15 | ggt Gly 385 | cga Arg | aca Thr | gtt Val | ttt Phe | tct Ser 390 | aat Asn | ggc Gly | tat Tyr | tca Ser | agc Ser 395 | ccc Pro | agc Ser | atg Met | aga Arg | cca Pro 400 | 1200 |
| 20 | gat Asp | gta Val | agc Ser | tct Ser | cct Pro 405 | cca Pro | tcc Ser | agc Ser | tcc Ser | tca Ser 410 | aca Thr | gca Ala | aca Thr | aca Thr | gga Gly 415 | cca Pro | 1248 |
| | cct Pro | ccc Pro | aaa Lys | ctc Leu 420 | tgc Cys | ctg Leu | gtg Val | tgc Cys | tct Ser 425 | gat Asp | gaa Glu | gct Ala | tca Ser | gga Gly 430 | tgt Cys | cat His | 1296 |
| 25 | | | | | | | | | | | | | | | | | |
| 30 | tat Tyr | gga Gly | gtc Val 435 | tta Leu | act Thr | tgt Cys | gga Gly | agc Ser 440 | tgt Cys | aaa Lys | gtt Val | ttc Phe | ttc Phe 445 | aaa Lys | aga Arg | gca Ala | 1344 |
| | gtg Val | gaa Glu 450 | gga Gly | cag Gln | cac His | aat Asn | tac Tyr 455 | cta Leu | tgt Cys | gct Ala | gga Gly | agg Arg 460 | aat Asn | gat Asp | tgc Cys | atc Ile | 1392 |
| 35 | atc Ile 465 | gat Asp | aaa Lys | att Ile | cga Arg | aga Arg 470 | aaa Lys | aac Asn | tgc Cys | cca Pro | gca Ala 475 | tgc Cys | cgc Arg | tat Tyr | cga Arg | aaa Lys 480 | 1440 |
| 40 | tgt Cys | ctt Leu | cag Gln | gct Ala | gga Gly 485 | atg Met | aac Asn | ctg Leu | gaa Glu | gct Ala 490 | cga Arg | aaa Lys | aca Thr | aag Lys | aaa Lys 495 | aaa Lys | 1488 |
| 45 | ata Ile | aaa Lys | gga Gly | att Ile 500 | cag Gln | cag Gln | gcc Ala | act Thr | aca Thr 505 | gga Gly | gtc Val | tca Ser | caa Gln | gaa Glu 510 | acc Thr | tct Ser | 1536 |
| 50 | gaa Glu | aat Asn | cct Pro 515 | ggt Gly | aac Asn | aaa Lys | aca Thr | ata Ile 520 | gtt Val | cct Pro | gca Ala | acg Thr | tta Leu 525 | cca Pro | caa Gln | ctc Leu | 1584 |
| 00 | acc Thr | cct Pro 530 | acc Thr | ctg Leu | gtg Val | tca Ser | ctg Leu 535 | ttg Leu | gag Glu | gtt Val | att Ile | gaa Glu 540 | cct Pro | gaa Glu | gtg Val | tta Leu | 1632 |
| 55 | tat Tyr 545 | gca Ala | gga Gly | tat Tyr | gat Asp | agc Ser 550 | tct Ser | gtt Val | cca Pro | gac Asp | tca Ser 555 | act Thr | tgg Trp | agg Arg | atc Ile | atg Met 560 | 1680 |
| 60 | act Thr | acg Thr | ctc Leu | aac Asn | atg Met 565 | tta Leu | gga Gly | ggg Gly | cgg Arg | caa Gln 570 | gtg Val | att Ile | gca Ala | gca Ala | gtg Val 575 | aaa Lys | 1728 |
| | tgg | gca | aag | gca | ata | cca | ggt | ttc | agg | aac | tta | cac | ctg | gat | gac | caa | 1776 |

| | Trp | Ala | Lys | Ala 580 | Ile | Pro | Gly | Phe | Arg 585 | Asn | Leu | His | Leu | Asp 590 | Asp | Gln | |
|----|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|------|
| 5 | atg Met | acc Thr | cta Leu 595 | ctg Leu | cag Gln | tac Tyr | tcc Ser | tgg Trp 600 | atg Met | tcc Ser | ctt Leu | atg Met | gca Ala 605 | ttt Phe | gct Ala | ctg Leu | 1824 |
| 10 | ggg | tgg Trp 610 | aga Arg | tca Ser | tat Tyr | aga Arg | caa Gln 615 | tca Ser | agt Ser | gca Ala | aac Asn | ctg Leu 620 | ctg Leu | tgt Cys | ttt Phe | gct Ala | 1872 |
| 15 | cct Pro 625 | gat Asp | ctg Leu | att Ile | att Ile | aat Asn 630 | gag Glu | cag Gln | aga Arg | atg Met | act Thr 635 | cta Leu | ccc Pro | tgc Cys | atg Met | tac Tyr 640 | 1920 |
| | gac Asp | caa Gln | tgt Cys | aaa Lys | cac His 645 | atg Met | ctg Leu | tat Tyr | gtt Val | tcc Ser 650 | tct Ser | gag Glu | tta Leu | cac His | agg Arg 655 | ctt Leu | 1968 |
| 20 | cag Gln | gta Val | tct Ser | tat Tyr 660 | gaa Glu | gag Glu | tat Tyr | ctc Leu | tgt Cys 665 | atg Met | aaa Lys | acc Thr | tta Leu | ctg Leu 670 | ctt Leu | ctc Leu | 2016 |
| 25 | tct Ser | tca Ser | gtt Val 675 | cct Pro | aag Lys | gac Asp | ggt Gly | ctg Leu 680 | aag Lys | agc Ser | caa Gln | gag Glu | cta Leu 685 | ttt Phe | gat Asp | gaa Glu | 2064 |
| 30 | att Ile | aga Arg 690 | atg Met | acc Thr | tac Tyr | atc Ile | aaa Lys 695 | gag Glu | cta Leu | gga Gly | aaa Lys | gcc Ala 700 | att Ile | gtc Val | aag Lys | agg Arg | 2112 |
| 35 | gaa Glu 705 | gga Gly | aac Asn | tcc Ser | agc Ser | cag Gln 710 | aac Asn | tgg Trp | cag Gln | cgg Arg | ttt Phe 715 | tat Tyr | caa Gln | ctg Leu | aca Thr | aaa Lys 720 | 2160 |
| 40 | ctc Leu | ttg Leu | gat Asp | tct Ser | atg Met 725 | cat His | gaa Glu | gtg Val | gtt Val | gaa Glu 730 | aat Asn | ctc Leu | ctt Leu | aac Asn | tat Tyr 735 | tgc Cys | 2208 |
| 45 | ttc Phe | caa Gln | aca Thr | ttt Phe 740 | ttg Leu | gat Asp | aag Lys | acc Thr | atg Met 745 | agt Ser | att Ile | gaa Glu | ttc Phe | ccc Pro 750 | gag Glu | atg Met | 2256 |
| | tta Leu | gct Ala | gaa Glu 755 | atc Ile | atc Ile | acc Thr | aat Asn | cag Gln 760 | ata Ile | cca Pro | aaa Lys | tat Tyr | tca Ser 765 | aat Asn | gga Gly | aat Asn | 2304 |
| 50 | atc Ile | aaa Lys 770 | aaa Lys | ctt Leu | ctg Leu | ttt Phe | cat His 775 | caa Gln | aag Lys | tga | | | | | | | 2334 |
| 55 | <210 |)> 4 | 1 | | | | | | | | | | | | | | |
| | <211 | i> 7 | 77 | | | | | | | | | | | | | | |
| 60 | <212 | 2> I | PRT | | | | | | | | | | | | | | |
| 50 | <213 | 3> F | Iomo | sapi | .ens | | | | | | | | | | | | |

<400> 4 5 Met Asp Ser Lys Glu Ser Leu Thr Pro Gly Arg Glu Glu Asn Pro Ser 10 Ser Val Leu Ala Gln Glu Arg Gly Asp Val Met Asp Phe Tyr Lys Thr 10 25 Leu Arg Gly Gly Ala Thr Val Lys Val Ser Ala Ser Ser Pro Ser Leu 15 Ala Val Ala Ser Gln Ser Asp Ser Lys Gln Arg Arg Leu Leu Val Asp 20 Phe Pro Lys Gly Ser Val Ser Asn Ala Gln Gln Pro Asp Leu Ser Lys 25 Ala Val Ser Leu Ser Met Gly Leu Tyr Met Gly Glu Thr Glu Thr Lys Val Met Gly Asn Asp Leu Gly Phe Pro Gln Gln Gly Gln Ile Ser Leu 30 Ser Ser Gly Glu Thr Asp Leu Lys Leu Glu Glu Ser Ile Ala Asn 35 Leu Asn Arg Ser Thr Ser Val Pro Glu Asn Pro Lys Ser Ser Ala Ser 135 40 Thr Ala Val Ser Ala Ala Pro Thr Glu Lys Glu Phe Pro Lys Thr His 150 155 160 45 Ser Asp Val Ser Ser Glu Gln Gln His Leu Lys Gly Gln Thr Gly Thr 165 170 50 Asn Gly Gly Asn Val Lys Leu Tyr Thr Thr Asp Gln Ser Thr Phe Asp Ile Leu Gln Asp Leu Glu Phe Ser Ser Gly Ser Pro Gly Lys Glu Thr 55 200 Asn Glu Ser Pro Trp Arg Ser Asp Leu Leu Ile Asp Glu Asn Cys Leu 60

Leu Ser Pro Leu Ala Gly Glu Asp Asp Ser Phe Leu Leu Glu Gly Asn

235

| 5 | Ser | Asn | Glu | Asp | Cys 245 | Lys | Pro | Leu | Ile | Leu 250 | Pro | Asp | Thr | Lys | Pro 255 | Lys |
|----|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|
| | Ile | Lys | Asp | Asn 260 | Gly | Asp | Leu | Val | Leu 265 | Ser | Ser | Pro | Ser | Asn 270 | Val | Thr |
| 10 | Leu | Pro | Gln 275 | Val | Lys | Thr | Glu | Lys 280 | Glu | Asp | Phe | Ile | Glu 285 | Leu | Cys | Thr |
| 15 | Pro | Gly 290 | Val | Ile | Lys | Gln | Glu 295 | Lys | Leu | Gly | Thr | Val 300 | Tyr | Cys | Gln | Ala |
| 20 | Ser 305 | Phe | Pro | Gly | Ala | Asn 310 | Ile | Ile | Gly | Asn | Lys 315 | Met | Ser | Ala | Ile | Ser 320 |
| 25 | Val | His | Gly | Val | Ser 325 | Thr | Ser | Gly | Gly | Gln 330 | Met | Tyr | His | Tyr | Asp 335 | Met |
| | Asn | Thr | Ala | Ser 340 | Leu | Ser | Gln | Gln | Gln 345 | Asp | Gln | Lys | Pro | 11e 350 | Phe | Asn |
| 30 | Val | Ile | Pro 355 | Pro | Ile | Pro | Val | Gly 360 | Ser | Glu | Asn | Trp | Asn 365 | Arg | Cys | Gln |
| 35 | | 370 | Gly | | | | 375 | | | | | 380 | | | | |
| 40 | Gly 385 | Arg | Thr | Val | Phe | Ser 390 | Asn | Gly | Tyr | Ser | Ser 395 | Pro | Ser | Met | Arg | Pro 400 |
| 40 | Asp | Val | Ser | Ser | Pro 405 | Pro | Ser | Ser | Ser | Ser 410 | Thr | Ala | Thr | Thr | Gly 415 | Pro |
| 45 | Pro | Pro | Lys | Leu 420 | Cys | Leu | Val | Cys | Ser 425 | Asp | Glu | Ala | Ser | Gly 430 | Cys | His |
| 50 | Tyr | Gly | Val 435 | Leu | Thr | Cys | Gly | Ser 440 | Cys | Lys | Val | Phe | Phe 445 | Lys | Arg | Ala |
| 55 | Val | Glu 450 | Gly | Gln | His | Asn | Tyr 455 | Leu | Суѕ | Ala | Gly | Arg 460 | Asn | Asp | Cys | Ile |
| | Ile 465 | Asp | Lys | Ile | Arg | Arg 470 | Lys | Asn | Cys | Pro | Ala 475 | Cys | Arg | Tyr | Arg | Lys 480 |
| 60 | Cys | Leu | Gln | Ala | Gly 485 | Met | Asn | Leu | Glu | Ala 490 | Arg | Lys | Thr | Lys | Lys 495 | Lys |

| | | | 500 | | | | | 505 | Gly | vui | OCI | 0111 | 510 | **** | 001 |
|------------|---|--|---|--|---|--|---|--|---|--|---|---|---|---|--|
| Glu | Asn | Pro 515 | Gly | Asn | Lys | Thr | Ile 520 | Val | Pro | Ala | Thr | Leu 525 | Pro | Gln | Leu |
| Thr | Pro 530 | Thr | Leu | Val | Ser | Leu 535 | Leu | Glu | Val | Ile | Glu 540 | Pro | Glu | Val | Leu |
| Tyr 545 | Ala | Gly | Tyr | Asp | Ser 550 | Ser | Val | Pro | Asp | Ser 555 | Thr | Trp | Arg | Ile | Met 560 |
| Thr | Thr | Leu | Asn | Met 565 | Leu | Gly | Gly | Arg | Gln 570 | Val | Ile | Ala | Ala | Val 575 | Lys |
| Trp | Ala | Lys | Ala 580 | Ile | Pro | Gly | Phe | Arg 585 | Asn | Leu | His | Leu | Asp 590 | Asp | Glr |
| Met | Thr | Leu 595 | Leu | Gln | Tyr | Ser | Trp 600 | Met | Ser | Leu | Met | Ala 605 | Phe | Ala | Leu |
| Gly | Trp 610 | Arg | Ser | Tyr | Arg | Gln 615 | Ser | Ser | Ala | Asn | Leu 620 | Leu | Cys | Phe | Ala |
| Pro 625 | Asp | Leu | Ile | Ile | Asn 630 | Glu | Gln | Arg | Met | Thr 635 | Leu | Pro | Cys | Met | Ту1 640 |
| Asp | Gln | Cys | Lys | His 645 | Met | Leu | Tyr | Val | Ser 650 | Ser | Glu | Leu | His | Arg 655 | Let |
| Gln | Val | Ser | Tyr 660 | Glu | Glu | Туг | Leu | Cys 665 | Met | Lys | Thr | Leu | Leu 670 | Leu | Leu |
| Ser | Ser | Val 675 | Pro | Lys | Asp | Gly | Leu 680 | Lys | Ser | Gln | Glu | Leu 685 | Phe | Asp | Glu |
| Ile | Arg 690 | Met | Thr | Tyr | Ile | Lys 695 | Glu | Leu | Gly | Lys | Ala 700 | Ile | Val | Lys | Arg |
| Glu 705 | Gly | Asn | Ser | Ser | Gln 710 | Asn | Trp | Gln | Arg | Phe 715 | Tyr | Gln | Leu | Thr | Lys 720 |
| Leu | Leu | Asp | Ser | Met 725 | His | Glu | Val | Val | Glu 730 | Asn | Leu | Leu | Asn | Туг 735 | Cys |
| Phe | Gln | Thr | Phe 740 | Leu | Asp | Lys | Thr | Met 745 | Ser | Ile | Glu | Phe | Pro 750 | Glu | Met |
| | Thr Tyr 545 Thr Trp Met Gly Pro 625 Asp Gln Ser Ile Glu 705 Leu | Thr Pro 530 Tyr Ala 545 Thr Thr Trp Ala Met Thr Gly Trp 610 Pro Asp 625 Asp Gln Gln Val Ser Ser Ile Arg 690 Glu Gly Tote Leu | Thr Pro Thr 530 Thr 545 Ala Gly Trp Ala Lys Arg Gln Cys Gln Val Ser Ser Val 675 Ile Arg Glu Glu Glu Glu Glu Glu Cys Leu Asp Leu Asp Leu Asp Leu Asp Met Glu Glu Gly Asn Cys Glu Gly Asn Cys Glu Cys Glu Cys Asp Glu Cys Glu Cys | Glu Asn Pro 515 Gly Thr Pro 530 Thr Leu Tyr Ala Gly Tyr Thr Leu Asn Trp Ala Lys Ala Gly Trp Arg Ser Pro Asp Leu Ile Asp Gln Cys Lys Gln Val Ser Tyr Gln Val Pro Glo Asp Pro Gla Asp Pro Gla Asp Ser Leu Leu Asp Ser Leu Leu Asp Ser Fer Gln Thr Thr Fer Gln Thr Thr Fer Gln Thr Thr Fer Gln Thr Thr Fer Thr Thr Thr Fer Thr Thr Thr Fer Thr Thr Thr Fer< | Glu Asn Pro 515 Gly Asn Thr Pro 530 Thr Leu Val Tyr Ala Gly Tyr Asp Thr Leu Asn Met Trp Ala Lys Ala Ile Met Thr Leu Leu Gln Gly Arg Ser Tyr Asp Leu Ile Ile Asp Cys Lys 645 Gln Cys Tyr 645 Gln Yal Pro Lys 645 Tyr 645 645 Gln Yal Pro Lys 645 Tyr Fro Lys 645 Tyr Fro Lys 610 Asn Pro Lys 61x Asn Pro Lys 61x Asn Ser Ser 61x Asn Ser Ser 61x Asn Ser Ser 61x | Glu Asn Pro 515 Gly Asn Lys Thr Pro 530 Thr Leu Val Ser Tyr Ala Gly Tyr Asp Ser Thr Thr Leu Asn Met Leu Trp Ala Lys Ala Tyr Arg Gly Trp Arg Ser Tyr Arg Asp Asp Leu Ile Ile Asn Asp Gln Cys Lys His Met Gln Val Ser Tyr Asp Gln Val Pro Lys Asp Gln Arg Pro Lys Asp Gln Arg Pro Lys Asp Ile Arg Met Thr Tyr Ile Glu Arg Arg Ser Ser Gln Thr Heu Leu Arg Ser Met Thr Tyr His He Leu </th <th>Glu Asn Pro Sins Gly Asn Lys Thr Thr 530 Thr Leu Val Ser 535 Tyr Ala Gly Tyr Asp Ser Ser Thr Thr Leu Asn Met Leu Gly Met Thr Leu Asn Tyr Arg Gly Met Thr Leu Gln Tyr Arg Gln Gly Asp Leu His Arg Glu Asp Cln Cys Lys His Met Leu Asp Cln Cys Lys His Met Leu Asp Cys Lys His Gly Tyr Ser Ser Tyr Glu Tyr Gly File Arg Met Thr Tyr Lu Lys Glu Gly Asn Ser File Asn Gly He Leu Asp Ser File</th> <th>Glu Asn Pro 515 Gly Asn Lys Thr 1le 520 Thr Pro 515 Gly Asn Lys Leu Leu Thr Pro 530 Thr Leu Val Ser Leu Leu Tyr Ala Gly Tyr Asp Ser Ser Yal Thr Thr Leu Asn Met Leu Gly Phe Met Thr Leu Asn Tyr Arg Gly Phe Gly Trp Arg Ser Tyr Arg Gly Pre Gly Trp Arg Leu His Met Leu Tyr Asp Glu Lys His Met Leu Tyr Glu Val Ser Tyr Glu Asp Glu Eu His Glu Asp Fre Glu Asp Trp Glu</th> <th>Glu Asn Pro 515 Gly Asn Lys Thr Ile Val 520 Thr Pro 530 Thr Leu Val Ser Leu Leu Glu Tyr Ala Gly Tyr Asp Ser Ser Val Pro Thr Thr Leu Asn Met Leu Gly Phe Arg Tr Ala Lys Ala Ile Pro Gly Phe Arg Met Thr Leu Leu Gln Tyr Ser Trp Met Gly Tr Arg Ser Tyr Arg Gln Ser Ser Fr Asp Leu Tyr Gas Glu Tyr Val Asp Gln Cys Gas Fyr Glu Tyr Leu Cys Gas Base Ser Val Pyr Fyr Fyr Fyr</th> <th>Glu Asn Pro 515 Gly Asn Lys Thr 11e Val Pro 520 Thr Pro 515 Thr Leu Val Ser Leu Glu Val Thr Pro 530 Thr Leu Val Ser Ser Leu Glu Pro Tyr Ala Gly Tyr Asp Ser Leu Gly Arg Arg Asp Met Thr Leu Asa Ile Pro Gly Phe Arg Asn Asp Thr Leu Glu Tyr Arg Glu Ser Asn Asp Leu Ile Ile Asp Glu Tyr Met Asp Glu Cys Lys Asp Glu Tyr Val Ser Asp Glu Cys Cys Asp Glu Leu Cys Met Asp Glu Asp Asp<!--</th--><th>Glu Asn Pro 515 Gly Asn Lys Thr Ile Val Pro Ala Thr Pro 530 Thr Leu Val Ser Leu Leu Val Ile Tyr Ala Gly Tyr Asp Ser Ser Val Pro Asp Ser Thr Thr Leu Asn Met Leu Gly Gly Arg Gln Val Trp Ala Lys Ala Ile Pro Gly Phe Arg Asn Leu Met Thr Leu Gln Tyr Ser Trp Met Ser Leu Gly Trp Arg Ser Tyr Arg Gln Ser Asn Asn Gly Trp Arg Glu Glu Glu Tyr Glu Glu Tyr Glu Leu Tyr Glu Leu Gly Lys</th><th>Glu Asn Pro Gly Asn Lys Thr Ile Val Pro Ala Thr Thr Pro Thr Leu Val Pro Ala Ile Glu Ser Thr Fro Ala Glu Pro Asp Ser Thr Pro Asp Ser Thr Pro Asp Ser Thr Pro Asp Ser Pro Pro Asp Ser Thr Pro Asp Ser Pro Asp Asp Ser Pro Asp Asp Asp Ile Pro Gly Pro Asp Asp Ile His Asp Ile Pro Gly Pro Asp Asp Ile Asp Ile Asp Ile Asp Ile Asp Ile Arg Asp Ile Asp Ile Ile Asp Ile Ile Ile Asp Ile Ile Ile Ile</th><th>Glu Asn Pro 515 Gly Asn Lys Thr 520 Val Pro Ala Thr Leu 525 Thr Pro 515 Thr Leu Val Ser Leu Glu Glu Val Ile 540 Pro 545 Tyr Ala Gly Tyr Asp Ser Ser Val Pro Asp Ser Tyr Thr Thr Leu Asn Met Leu Gly Gly Pro Arg Ann Leu His Leu Ala Trp Ala Lys Ala Ile Pro Gly Pro Arg Ann Leu His Leu Ala Met Thr Leu Gly Tyr Ser Tyr Arg Met Ann Leu His Leu Ala Gly Trp Arg Ann Tyr Ser Tyr Ann Ann</th><th>Glu Asn Pro Gly Asn Lys Thr 11e Val Pro Ala Thr Leu Pro 525 Thr Pro Thr Leu Val Ser Leu Glu Val Ile Glu Pro Glu 545 Tyr Ala Gly Tyr Asp Ser Ser Val Pro Asp Ser Thr Trp Arg 545 Thr Thr Leu Asn Met Set Gly Phe Arg Asn Leu His Ala Ala 586 Trp Ala Lys Ala Ile Pro Gly Phe Arg Asn Leu Met Ala Phe 595 Met Thr Leu Leu Gln Tyr Asp Gln Ser Ser Ala Asn Leu Met Ala Phe 605 Gly Trp Arg Ser Tyr Arg Gln Ser Ser Ala Asn Leu Met Ala Phe 625 Asp Gln Cys Lys His Met Leu Tyr Val Ser Glu Leu His 645 Gln Val Ser Tyr Glu Glu Tyr Leu Cys 665 Gln Val Ser Tyr Glu Glu Tyr Leu Cys 665 The Arg Met Thr Tyr Ile Lys Glu Leu Gly Lys Thr Leu Leu Gyo Glu Glu Asn Trp Gln Arg Phe 770 Glu Gly Asn Ser Ser Gln Asn Trp Gln Arg Phe Tyr Gln Leu Phe 680 Glu Gly Asn Ser Ser Gln Asn Trp Gln Arg Phe Tyr Gln Leu Phe 680 Glu Gly Asn Ser Ser Gln Asn Trp Gln Arg Phe Tyr Gln Leu Asn 770 Fee Gln Thr Phe Leu Asp Lys Thr Met Ser Ile Glu Phe Pro</th><th>Glu Asn Pro Gly Asn Lys Thr Jle Val Pro Ala Thr Leu Pro Gln S155 Thr Pro Thr Leu Val Ser Leu Leu Glu Val Ile Glu Pro Glu Val S155 Thr Thr Leu Asn Met Leu Gly Gly Asn Leu His Leu Asp Asp S55 Thr S550 Asn Leu His Leu Asp Asp Asp Asp S550 Asn Leu His Leu Cys Phe G10 Arg Asp Leu Ile Ile Asn G11 Ser Ser Ala Asn Leu Leu Cys Phe G25 Asp Leu Ile Ile Asn G11 Gln Arg Met Thr Leu Pro Cys Met G25 Asp Leu Ile Ile Asn G11 Tyr Leu Cys Met G35 Lys Thr Leu Leu Leu Leu Cys Met G45 Gln Val Ser Tyr G45 Glu G10 Tyr Leu Cys Met G55 Asp Cal Leu His Arg G45 Gln Val Ser Tyr G10 Asp G10 G10 G10 Tyr Leu Cys Met G55 Asp Met Tyr Leu Cys Met G55 Asp Met Tyr Leu Cys Met G55 Asp Met Tyr Leu Cys Met G55 G10 G10 G10 G10 G10 G10 G10 G10 G10 G10</th></th> | Glu Asn Pro Sins Gly Asn Lys Thr Thr 530 Thr Leu Val Ser 535 Tyr Ala Gly Tyr Asp Ser Ser Thr Thr Leu Asn Met Leu Gly Met Thr Leu Asn Tyr Arg Gly Met Thr Leu Gln Tyr Arg Gln Gly Asp Leu His Arg Glu Asp Cln Cys Lys His Met Leu Asp Cln Cys Lys His Met Leu Asp Cys Lys His Gly Tyr Ser Ser Tyr Glu Tyr Gly File Arg Met Thr Tyr Lu Lys Glu Gly Asn Ser File Asn Gly He Leu Asp Ser File | Glu Asn Pro 515 Gly Asn Lys Thr 1le 520 Thr Pro 515 Gly Asn Lys Leu Leu Thr Pro 530 Thr Leu Val Ser Leu Leu Tyr Ala Gly Tyr Asp Ser Ser Yal Thr Thr Leu Asn Met Leu Gly Phe Met Thr Leu Asn Tyr Arg Gly Phe Gly Trp Arg Ser Tyr Arg Gly Pre Gly Trp Arg Leu His Met Leu Tyr Asp Glu Lys His Met Leu Tyr Glu Val Ser Tyr Glu Asp Glu Eu His Glu Asp Fre Glu Asp Trp Glu | Glu Asn Pro 515 Gly Asn Lys Thr Ile Val 520 Thr Pro 530 Thr Leu Val Ser Leu Leu Glu Tyr Ala Gly Tyr Asp Ser Ser Val Pro Thr Thr Leu Asn Met Leu Gly Phe Arg Tr Ala Lys Ala Ile Pro Gly Phe Arg Met Thr Leu Leu Gln Tyr Ser Trp Met Gly Tr Arg Ser Tyr Arg Gln Ser Ser Fr Asp Leu Tyr Gas Glu Tyr Val Asp Gln Cys Gas Fyr Glu Tyr Leu Cys Gas Base Ser Val Pyr Fyr Fyr Fyr | Glu Asn Pro 515 Gly Asn Lys Thr 11e Val Pro 520 Thr Pro 515 Thr Leu Val Ser Leu Glu Val Thr Pro 530 Thr Leu Val Ser Ser Leu Glu Pro Tyr Ala Gly Tyr Asp Ser Leu Gly Arg Arg Asp Met Thr Leu Asa Ile Pro Gly Phe Arg Asn Asp Thr Leu Glu Tyr Arg Glu Ser Asn Asp Leu Ile Ile Asp Glu Tyr Met Asp Glu Cys Lys Asp Glu Tyr Val Ser Asp Glu Cys Cys Asp Glu Leu Cys Met Asp Glu Asp Asp </th <th>Glu Asn Pro 515 Gly Asn Lys Thr Ile Val Pro Ala Thr Pro 530 Thr Leu Val Ser Leu Leu Val Ile Tyr Ala Gly Tyr Asp Ser Ser Val Pro Asp Ser Thr Thr Leu Asn Met Leu Gly Gly Arg Gln Val Trp Ala Lys Ala Ile Pro Gly Phe Arg Asn Leu Met Thr Leu Gln Tyr Ser Trp Met Ser Leu Gly Trp Arg Ser Tyr Arg Gln Ser Asn Asn Gly Trp Arg Glu Glu Glu Tyr Glu Glu Tyr Glu Leu Tyr Glu Leu Gly Lys</th> <th>Glu Asn Pro Gly Asn Lys Thr Ile Val Pro Ala Thr Thr Pro Thr Leu Val Pro Ala Ile Glu Ser Thr Fro Ala Glu Pro Asp Ser Thr Pro Asp Ser Thr Pro Asp Ser Thr Pro Asp Ser Pro Pro Asp Ser Thr Pro Asp Ser Pro Asp Asp Ser Pro Asp Asp Asp Ile Pro Gly Pro Asp Asp Ile His Asp Ile Pro Gly Pro Asp Asp Ile Asp Ile Asp Ile Asp Ile Asp Ile Arg Asp Ile Asp Ile Ile Asp Ile Ile Ile Asp Ile Ile Ile Ile</th> <th>Glu Asn Pro 515 Gly Asn Lys Thr 520 Val Pro Ala Thr Leu 525 Thr Pro 515 Thr Leu Val Ser Leu Glu Glu Val Ile 540 Pro 545 Tyr Ala Gly Tyr Asp Ser Ser Val Pro Asp Ser Tyr Thr Thr Leu Asn Met Leu Gly Gly Pro Arg Ann Leu His Leu Ala Trp Ala Lys Ala Ile Pro Gly Pro Arg Ann Leu His Leu Ala Met Thr Leu Gly Tyr Ser Tyr Arg Met Ann Leu His Leu Ala Gly Trp Arg Ann Tyr Ser Tyr Ann Ann</th> <th>Glu Asn Pro Gly Asn Lys Thr 11e Val Pro Ala Thr Leu Pro 525 Thr Pro Thr Leu Val Ser Leu Glu Val Ile Glu Pro Glu 545 Tyr Ala Gly Tyr Asp Ser Ser Val Pro Asp Ser Thr Trp Arg 545 Thr Thr Leu Asn Met Set Gly Phe Arg Asn Leu His Ala Ala 586 Trp Ala Lys Ala Ile Pro Gly Phe Arg Asn Leu Met Ala Phe 595 Met Thr Leu Leu Gln Tyr Asp Gln Ser Ser Ala Asn Leu Met Ala Phe 605 Gly Trp Arg Ser Tyr Arg Gln Ser Ser Ala Asn Leu Met Ala Phe 625 Asp Gln Cys Lys His Met Leu Tyr Val Ser Glu Leu His 645 Gln Val Ser Tyr Glu Glu Tyr Leu Cys 665 Gln Val Ser Tyr Glu Glu Tyr Leu Cys 665 The Arg Met Thr Tyr Ile Lys Glu Leu Gly Lys Thr Leu Leu Gyo Glu Glu Asn Trp Gln Arg Phe 770 Glu Gly Asn Ser Ser Gln Asn Trp Gln Arg Phe Tyr Gln Leu Phe 680 Glu Gly Asn Ser Ser Gln Asn Trp Gln Arg Phe Tyr Gln Leu Phe 680 Glu Gly Asn Ser Ser Gln Asn Trp Gln Arg Phe Tyr Gln Leu Asn 770 Fee Gln Thr Phe Leu Asp Lys Thr Met Ser Ile Glu Phe Pro</th> <th>Glu Asn Pro Gly Asn Lys Thr Jle Val Pro Ala Thr Leu Pro Gln S155 Thr Pro Thr Leu Val Ser Leu Leu Glu Val Ile Glu Pro Glu Val S155 Thr Thr Leu Asn Met Leu Gly Gly Asn Leu His Leu Asp Asp S55 Thr S550 Asn Leu His Leu Asp Asp Asp Asp S550 Asn Leu His Leu Cys Phe G10 Arg Asp Leu Ile Ile Asn G11 Ser Ser Ala Asn Leu Leu Cys Phe G25 Asp Leu Ile Ile Asn G11 Gln Arg Met Thr Leu Pro Cys Met G25 Asp Leu Ile Ile Asn G11 Tyr Leu Cys Met G35 Lys Thr Leu Leu Leu Leu Cys Met G45 Gln Val Ser Tyr G45 Glu G10 Tyr Leu Cys Met G55 Asp Cal Leu His Arg G45 Gln Val Ser Tyr G10 Asp G10 G10 G10 Tyr Leu Cys Met G55 Asp Met Tyr Leu Cys Met G55 Asp Met Tyr Leu Cys Met G55 Asp Met Tyr Leu Cys Met G55 G10 G10 G10 G10 G10 G10 G10 G10 G10 G10</th> | Glu Asn Pro 515 Gly Asn Lys Thr Ile Val Pro Ala Thr Pro 530 Thr Leu Val Ser Leu Leu Val Ile Tyr Ala Gly Tyr Asp Ser Ser Val Pro Asp Ser Thr Thr Leu Asn Met Leu Gly Gly Arg Gln Val Trp Ala Lys Ala Ile Pro Gly Phe Arg Asn Leu Met Thr Leu Gln Tyr Ser Trp Met Ser Leu Gly Trp Arg Ser Tyr Arg Gln Ser Asn Asn Gly Trp Arg Glu Glu Glu Tyr Glu Glu Tyr Glu Leu Tyr Glu Leu Gly Lys | Glu Asn Pro Gly Asn Lys Thr Ile Val Pro Ala Thr Thr Pro Thr Leu Val Pro Ala Ile Glu Ser Thr Fro Ala Glu Pro Asp Ser Thr Pro Asp Ser Thr Pro Asp Ser Thr Pro Asp Ser Pro Pro Asp Ser Thr Pro Asp Ser Pro Asp Asp Ser Pro Asp Asp Asp Ile Pro Gly Pro Asp Asp Ile His Asp Ile Pro Gly Pro Asp Asp Ile Asp Ile Asp Ile Asp Ile Asp Ile Arg Asp Ile Asp Ile Ile Asp Ile Ile Ile Asp Ile Ile Ile Ile | Glu Asn Pro 515 Gly Asn Lys Thr 520 Val Pro Ala Thr Leu 525 Thr Pro 515 Thr Leu Val Ser Leu Glu Glu Val Ile 540 Pro 545 Tyr Ala Gly Tyr Asp Ser Ser Val Pro Asp Ser Tyr Thr Thr Leu Asn Met Leu Gly Gly Pro Arg Ann Leu His Leu Ala Trp Ala Lys Ala Ile Pro Gly Pro Arg Ann Leu His Leu Ala Met Thr Leu Gly Tyr Ser Tyr Arg Met Ann Leu His Leu Ala Gly Trp Arg Ann Tyr Ser Tyr Ann Ann | Glu Asn Pro Gly Asn Lys Thr 11e Val Pro Ala Thr Leu Pro 525 Thr Pro Thr Leu Val Ser Leu Glu Val Ile Glu Pro Glu 545 Tyr Ala Gly Tyr Asp Ser Ser Val Pro Asp Ser Thr Trp Arg 545 Thr Thr Leu Asn Met Set Gly Phe Arg Asn Leu His Ala Ala 586 Trp Ala Lys Ala Ile Pro Gly Phe Arg Asn Leu Met Ala Phe 595 Met Thr Leu Leu Gln Tyr Asp Gln Ser Ser Ala Asn Leu Met Ala Phe 605 Gly Trp Arg Ser Tyr Arg Gln Ser Ser Ala Asn Leu Met Ala Phe 625 Asp Gln Cys Lys His Met Leu Tyr Val Ser Glu Leu His 645 Gln Val Ser Tyr Glu Glu Tyr Leu Cys 665 Gln Val Ser Tyr Glu Glu Tyr Leu Cys 665 The Arg Met Thr Tyr Ile Lys Glu Leu Gly Lys Thr Leu Leu Gyo Glu Glu Asn Trp Gln Arg Phe 770 Glu Gly Asn Ser Ser Gln Asn Trp Gln Arg Phe Tyr Gln Leu Phe 680 Glu Gly Asn Ser Ser Gln Asn Trp 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| | Leu Ala Glu 755 | | Thr Asn Glr 760 | | Lys Tyr Ser 765 | Asn Gly Asn | |
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| 40 | | | | _ | ctc aac atg Leu Asn Met 45 | tta gga ggg Leu Gly Gly | 144 |
| 45 | | | | | aag gca ata Lys Ala Ile 60 | cca ggt ttc Pro Gly Phe | 192 |
| 50 | | His Leu A | - | - | cta ctg cag Leu Leu Gln 75 | | 240 |
| | _ | | | | aga tca tat Arg Ser Tyr | aga caa tca Arg Gln Ser 95 | 288 |
| 55 | | | - | _ | _ | aat gag cag Asn Glu Gln 110 | 336 |
| 60 | | Leu Pro C | | Asp Gln | | atg ctg tat Met Leu Tyr | 384 |
| | gtt tcc tct | gag tta c | cac agg cti | cag gta | tct tat gaa | gag tat ctc | 432 |

| | Val | Ser 130 | Ser | Glu | Leu | His | Arg 135 | Leu | Gln | Val | Ser | Tyr 140 | Glu | Glu | Tyr | Leu | |
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| 5 | tgt Cys 145 | atg Met | aaa Lys | acc Thr | tta Leu | ctg Leu 150 | ctt Leu | ctc Leu | tct Ser | tca Ser | gtt Val 155 | cct Pro | aag Lys | gac Asp | ggt Gly | ctg Leu 160 | 480 |
| 10 | aag Lys | agc Ser | caa Gln | gag Glu | cta Leu 165 | ttt Phe | gat Asp | gaa Glu | att Ile | aga Arg 170 | atg Met | acc Thr | tac Tyr | atc Ile | aaa Lys 175 | gag Glu | 528 |
| 15 | cta Leu | gga Gly | aaa Lys | gcc Ala 180 | att Ile | gtc Val | aag Lys | agg Arg | gaa Glu 185 | gga Gly | aac Asn | tcc Ser | agc Ser | cag Gln 190 | aac Asn | tgg Trp | 576 |
| | cag Gln | cgg Arg | ttt Phe 195 | tat Tyr | caa Gln | ctg Leu | aca Thr | aaa Lys 200 | ctc Leu | ttg Leu | gat Asp | tct Ser | atg Met 205 | cat His | gaa Glu | gtg Val | 624 |
| 20 | gtt Val | gaa Glu 210 | aat Asn | ctc Leu | ctt Leu | aac Asn | tat Tyr 215 | tgc Cys | ttc Phe | caa Gln | aca Thr | ttt Phe 220 | ttg Leu | gat Asp | aag Lys | acc Thr | 672 |
| 25 | | | | gaa Glu | | | | | | | | | | | | | 720 |
| 30 | | | | tat Tyr | | | | | | | | | | | | | 768 |
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| 50 | Glu | Val | Ile | Glu 20 | Pro | Glu | Val | Leu | Tyr 25 | Ala | Gly | Tyr | Asp | Ser 30 | Ser | Val | |
| 55 | Pro | Asp | Ser 35 | Thr | Trp | Arg | Ile | Met 40 | Thr | Thr | Leu | Asn | Met 45 | Leu | Gly | Gly | |
| 60 | Arg | Gln 50 | Val | Ile | Ala | Ala | Val 55 | Lys | Trp | Ala | Lys | Ala 60 | Ile | Pro | Gly | Phe | |
| | Arg | Asn | Leu | His | Leu | Asp | Asp | Gln | Met | Thr | Leu | Leu | Gln | Tyr | Ser | Trp | |

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| | 65 | | | | | 70 | | | | | 75 | | | | | 80 |
|-----|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|
| 5 | Met | Phe | Leu | Met | Ala 85 | Phe | Ala | Leu | Gly | Trp 90 | Arg | Ser | Tyr | Arg | Gln 95 | Ser |
| 10 | Ser | Ala | Asn | Leu 100 | Leu | Cys | Phe | Ala | Pro 105 | Asp | Leu | Ile | Ile | Asn 110 | Glu | Glr |
| | Arg | Met | Thr 115 | Leu | Pro | Cys | Met | Tyr 120 | Asp | Gln | Cys | Lys | His 125 | Met | Leu | Туг |
| 15 | Val | Ser 130 | Ser | Glu | Leu | His | Arg 135 | Leu | Gln | Val | Ser | Tyr 140 | Glu | Glu | Tyr | Let |
| 20 | Cys 145 | Met | Lys | Thr | Leu | Leu 150 | Leu | Leu | Ser | Ser | Val 155 | Pro | Lys | Asp | Gly | Leu 160 |
| 25 | Lys | Ser | Gln | Glu | Leu 165 | Phe | Asp | Glu | Ile | Arg 170 | Met | Thr | Tyr | Ile | Lys 175 | Glu |
| 30 | Leu | Gly | Lys | Ala 180 | Ile | Val | Lys | Arg | Glu 185 | Gly | Asn | Ser | Ser | Gln 190 | Asn | Trp |
| 0.5 | Gln | Arg | Phe 195 | Tyr | Gln | Leu | Thr | Lys 200 | Leu | Leu | Asp | Ser | Met 205 | His | Glu | Val |
| 35 | Val | Glu 210 | Asn | Leu | Leu | Asn | Tyr 215 | Cys | Phe | Gln | Thr | Phe 220 | Leu | Asp | Lys | Thr |
| 40 | Met 225 | Ser | Ile | Glu | Phe | Pro 230 | Glu | Met | Leu | Ala | Glu 235 | Ile | Ile | Thr | Asn | Glr 240 |
| 45 | Ile | Pro | Lys | Tyr | Ser 245 | Asn | Gly | Asn | Ile | Lys 250 | Lys | Leu | Leu | Phe | His 255 | Glr |
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| | gtt gaa Val Glu 210 | aat Asn | ctc Leu | ctt Leu | aac Asn | tat Tyr 215 | tgc Cys | ttc Phe | caa Gln | aca Thr | ttt Phe 220 | ttg Leu | gat Asp | aag Lys | acc Thr | 672 |
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| 10 | ata cca Ile Pro | aaa Lys | tat Tyr | tca Ser 245 | aat Asn | gga Gly | aat Asn | atc Ile | aaa Lys 250 | aaa Lys | ctt Leu | ctg Leu | ttt Phe | cat His 255 | caa Gln | 768 |
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| 40 | Pro Asp | Ser 35 | Thr | Trp | Arg | Ile | Met 40 | Thr | Thr | Leu | Asn | Met 45 | Leu | Gly | Gly | |
| | Arg Gln 50 | Val | Ile | Ala | Ala | Val 55 | Lys | Trp | Ala | Lys | Ala 60 | Ile | Pro | Gly | Phe | |
| 45 | Arg Asn 65 | Leu | His | Leu | Asp 70 | Asp | Gln | Met | Thr | Leu 75 | Leu | Gln | Tyr | Ser | Trp 80 | |
| 50 | Met Ser | Leu | Met | Ala 85 | Phe | Ala | Leu | Gly | Trp 90 | Arg | Ser | Tyr | Arg | Gln 95 | Ser | |
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| 60 | Arg Met | Thr 115 | Leu | Pro | Cys | Met | Tyr 120 | Asp | Gln | Cys | Lys | His 125 | Met | Leu | Tyr | |
| | Val Ser | Ser | Glu | Leu | His | Arg | Leu | Gln | Val | Ser | Tyr | Glu | Glu | Tyr | Leu | |

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| | | 130 | | | | | 135 | | | | | 140 | | | | |
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| 5 | Cys 145 | Met | Lys | Thr | Leu | Leu 150 | Leu | Leu | Ser | Ser | Val 155 | Pro | Lys | Asp | Gly | Leu 160 |
| 10 | Lys | Ser | Gln | Glu | Leu 165 | Phe | Asp | Glu | Ile | Arg 170 | Met | Thr | Tyr | Ile | Lys 175 | Glu |
| | Leu | Gly | Lys | Ala 180 | Ile | Val | Lys | Arg | Glu 185 | Gly | Asn | Ser | Ser | Gln 190 | Asn | Trp |
| 15 | Gln | Arg | Phe 195 | Tyr | Gln | Leu | Thr | Lys 200 | Leu | Leu | Asp | Ser | Met 205 | His | Glu | Val |
| 20 | Val | Glu 210 | Asn | Leu | Leu | Asn | Tyr 215 | Cys | Phe | Gln | Thr | Phe 220 | Leu | Asp | Lys | Thr |
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